



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :

Shirou SAWA :

Serial No.: NEW :

Filed June 23, 2003 :

**For: METHOD FOR STABILIZING ARYLCARBOXYLIC
ACID, STABILIZER THEREOF AND AQUEOUS
SOLUTION CONTAINING STABLIZED
ARYLCARBOXYLIC ACID**

**(Rule 1.53(b) continuation of Serial No. 09/885,096,
Filed June 21, 2001)**

DECLARATION UNDER 37 CFR 1.132

Honorable Commissioner of Patents and Trademarks

Washington, D. C. 20231

Sir:

I, Shirou Sawa, do hereby solemnly and sincerely declare that I am a citizen of Japan,
residing at 366-1, Minamibefu 4-chome, Nishi-ku, Kobe-shi, Hyogo 651-2116 Japan;

That my education and employment history is as follows:

I was graduated from The University of Tokushima, Graduate School of
Engineering in March, 1990. Since April, 1990 I have been employed by Senju
Pharmaceutical Co., Ltd., the assignee of the above-identified application, where
I have been engaged in research relating to pharmaceuticals;

That I am the inventor of the above-identified application and conducted the following
experiment;

EXPERIMENT

Stabilization of bromfenac sodium

Solutions (recipes 1-3 of Table 1 below) of 0.1w/v% bromfenac sodium were respectively charged in 5 ml colorless polypropylene container, allowed to stand at 60°C for 2 and 4 weeks. The percentage of residual bromfenac sodium in the polypropylene container after standing was determined by high performance liquid chromatography. The results are shown in Table 2. The values in Table 2 are relative to the amount of bromfenac sodium when it was prepared, which was taken as 100.

Table 1

Recipe No.	Rp.01	Rp.02	Rp.03
Bromfenac sodium	0.1 g	0.1 g	0.1 g
Boric acid	1.5 g	1.5 g	1.5 g
Benzalkonium chloride	0.005g	0.005g	0.005g
Polysorbate 80	0.15 g	0.15 g	0.15 g
Ofloxacin	—	0.3 g	—
Norfloxacin	—	—	0.1 g
Sodium hydroxide	q.s.	q.s.	q.s.
Total amount	100 mL	100 mL	100 mL
PH	8.2	8.2	8.2

Table 2

60°C2W	%	95.9	98.8	98.3
	Remaining			
60°C4W	Appearance	+	—	—
	%	93.6	97.2	96.1
	Remaining			
	Appearance	+	±	±

— : No precipitate was formed (Clear solution).

— : A great amount of red precipitate was formed (The precipitate of bromfenac sodium is red).

± : A very small amount of precipitate was formed (Whether or not the precipitate was red was not discernible) .

As is evident from the results shown in Table 2, bromfenac sodium was stabilized against heat by the addition of ofloxacin and norfloxacin (The residual bromfenc sodium was 2.4%-3.6% higher.) The precipitation of bromfenac sodium was also inhibited by the addition of ofloxacin and norfloxacin.

I, the undersigned, further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signed this *2nd* day of September, 2003

Shirou Sawa

Shirou Sawa